

NANOCAPSULES: A NOVEL DRUG DELIVERY SYSTEM

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ABSTRACT:

Nanocapsule ranges beginning 10nm to1000nm. They consist of liquid or solid core in which the drug is placed into cavity, Nano capsules are vesicular systems in which the drug is limited to a cavity consisting of an inner liquid core surrounded by a polymeric membrane. two types of polymers are used for preparation of nanocapsules they are natural, synthetic polymer. There are various methods are used for the preparation of nanocapsules like polymer absorption method, Nanoprecipitation/solvent displacement method, Double emulsification method, emulsion coacervation method, polymer coating method, layer-by-layer method. There is different characterization are performed to Nano capsules. Also, there are some applications are given it. Drug-loaded polymeric nanocapsules have showed possible applications The nanocapsules have various advantages and disadvantages. There are some benefits of nanocapsules. The capsules have some important properties the last there are characterization of nanocapsules.

KEYWORDS: Nanocapsule, polymer, drug delivery, delivery system, synthetic polymer

INTRODUCTION:

The drug candidate those having poor water solubility, which affect bioavailability and therapeutic index significantly, Nanoscale drug delivery systems have been great potential for enhancing the bioavailability of poorly water-soluble drugs and to increase the solubility, stability and permeation of drugs.

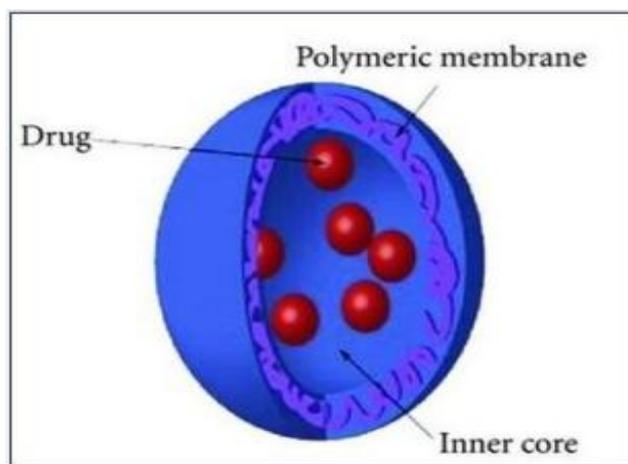


Fig 1: Nanocapsule

Current nanocarriers for drug delivery systems includes liposomes, nano emulsion, nanocrystals, nanoparticles and soon. Nano capsule can be referred as hollow polymer nanostructures. Nano capsule can serve as nano-sized drug carriers to achieve controlled release as well as efficient drug targeting. The dispersion stability and the physiological response are depending on surfactant used and the nature of the outer coating that is polymer used in the nano capsules preparation. Nano capsules have been developed as drug delivery systems for several drugs by different routes of administration such as oral and parenteral. They reduced the toxicity of drugs and improve the stability of drugs. [22] Other advantage of nano encapsulated systems as active substance carrier includes high drug encapsulation efficiency, low polymer content compared to other nanoparticulated systems such as nanosphere. Methods are used for the preparation of nano capsules are nanoprecipitation, emulsion co-acervation, emulsion diffusion, polymer coating, layer by layer. The characterization of nano capsules is done by using different techniques the particle size measured by dynamic light scattering, surface properties by using Zettaliter. [1] Nanotechnology is a science of small. Nano capsules, as characteristic class of nanoparticles. Nano derives from the Greek word "Nano" which means dwarf/small.[23] Their size ranges from 10nm to 1000 nm. In science and technology 'nano' stands for the order of magnitude 10^{-9} and thus describes very small dimension units between 'micro' (μ , 10^{-6}) and 'Pico' (p, 10^{-12}). Hence, 1 nm is equal to 10^{-9} m.

They are made up of one or more active materials core and a protective matrix shell.[24] In which the therapeutic substance may be limited. Nano capsules have been developed as drug delivery systems for several drugs by different routes of administrations such as oral and a rental. Decrease the toxicity of drugs. when polymeric nanoparticles contain a polymeric wall composed of non-ionic surfactants, macromolecules, phospholipids and an oil core they are names as “Nano capsules. Nano capsules, as typical class of nanoparticles, are made up of one or more active materials core and a protective matrix shell in which the therapeutic substance may be limited. Nano capsules take developed as drug delivery systems for several drugs by different routes of administrations such as oral and parental. Decrease the toxicity of drugs. Polymeric nanoparticles are named nano capsules when they contain a polymeric wall composed of non-ionic surfactants, macromolecules, phospholipids and an oil core they are names as “Nano capsules”. [2] A nano capsule consists of shell and a space in which desired substances may be placed. Nano capsules have more diagnostic and therapeutic potential and thus have demonstrated neuroprotective potential in vitro. Nano capsules having many advantages and disadvantages. Preparation of the nano capsules are used as two types of polymers 1) Natural polymers 2) Synthetic polymers. Nano capsules, as main class of nanoparticles, are made up of one or more active materials core and a protective matrix shell in which the therapeutic substance may be limited. Nano capsules mainly developed as drug delivery systems for several drugs by different routes of administrations such as oral and parental. Decrease the toxicity of drugs. [3] Nano capsules take developed as drug delivery systems for several drugs by different routes of administrations such as oral and parental. Decrease the toxicity of drugs. Polymeric nanoparticles are named nano capsules when they contain a polymeric wall composed of non-ionic surfactants, macromolecules, phospholipids and an oil core [4] Lipid nano capsule (LNCs) are nanoparticles prepared by a solvent free, low-energy phase inversion method and consist of an oily core composed of medium chain triglycerides which is enclosed by a layer of hydrophilic and hydrophobic surface tents The components of LNCs are pharmaceutically acceptable and are regarded as generally recognized as safe (i.e., are included in FDA’s GRAS list), and pharmacopoeia grades are commercially available. The characteristics of these nanoparticles can be adjusted to suit various applications with a possibility of loading both hydrophobic and hydro phallic drugs _Previous studies on LNCs demonstrated their potential for loading various actives for drug delivery (e.g., ibuprofen, amiodarone, tripe tone, paclitaxel, docetaxel, tamoxifen, cisplatin, and antimicrobial peptides) and their suitability for various administration routes like oral, dermal, pulmonal and parenteral including ocular routes. [5]

DEFINATION OF NANOCAPSULE:

First of all, the Nanocapsule can be related to vesicular systems in which a drug is kept in a cavity consisting of an inner lid aid core surrounded by a polymeric membrane. but seen from a general level, they can be defined as nano-vesicular systems that show a typical core-shell structure in which the drug is kept to a tank or within a cavity surrounded by a polymer membrane or coating. The cavity can cover the active substance in liquid or solid form or as per a molecular dispersion Also, this tank can be lipophilic or hydrophobic according to the preparation method and raw materials used. Also, interested in account the operative limitations of preparation methods, nanocapsules can also bring the active substance on their surfaces or consumed in the polymeric membrane. [6]

DEFINATION OF POLYMER:

“Polymers are long chain organic molecules collected from many smaller molecules called as monomers.”

In pharmaceutical preparations also they have several applications in mfg. of bottles, syringes, vials, catheters, and also in drug formulation.[9]

CLASSIFICATION OF POLYMERS:

❖ **Based On origin:**

- a) Natural Of Polymers: e.g., Proteins-collagen, Keratin, Albumin Carbohydrates-Starch
- b) Synthetic Polymers: e.g., Polystes, Polanhydrides, Polyamides

❖ **Based On Bio-Stability:**

- a) Bio-degrandable Polymer: e.g., Polyester, Proteins, Carbohydrates, etc.
- b) Non-biodegradable Polymer: e.g., Ethyl cellulose, HPMC, acrylic polymer.[9]

❖ **Natural Polymer:**

- Natural polymers are the substances which are found by natural sources like plant and animal sources.
- Proteins, enzymes, muscle fibers, polymer polysaccharide, sticky transudes are the natural polymers which are used in formulating pharmaceutical products.
- The famous natural polymers are chitosan, carrageenan, isapghula, acacia, gelatine, agar, shellac, guar gum.

- The detailed application of plant resulting polymer in pharmaceutical formulations include their use in the manufacture of solid monolithic matrix systems, implants, films, beads, micro particles, nanoparticles, inhalable and injectable system as well as viscous liquid formulations. [10]
- The most commonly used natural polymers are.

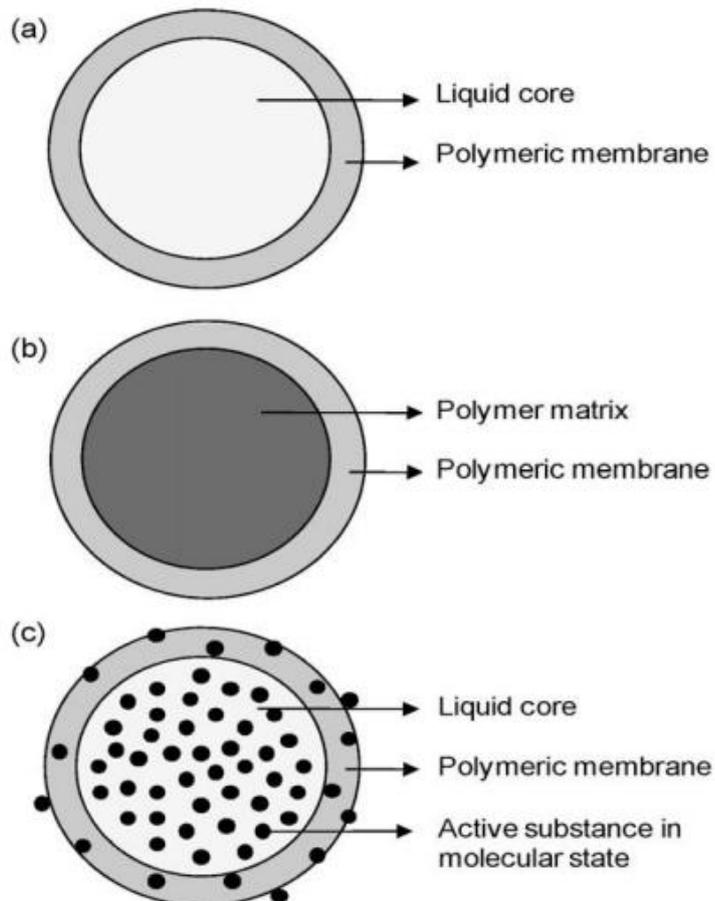


Fig 2: Polymer Based Nanocapsules

❖ Synthetic polymer

- Synthetic polymers are industrially produced chemical substances consisting of a number of molecules linked together with covalent bond.
- A wide variety of synthetic polymers are available with difference in main chain as well as side chain.
- The utmost commonly used synthetic polymer are polythene and polystyrene.

The most commonly used synthetic polymers are:

- 1) Polylactides (PLA).
- 2) Polyanhydrides
- 3) Polyglycolides (PGA)
- 4) Poly orthoesters
- 5) Poly lactide co-glycolides (PLGA)
- 6) Poly glutamic acid
- 7) Poly cyanoacrylates
- 8) Poly malic acid
- 9) Poly caprolactone
- 10) Poly methacrylic acid
- 11) Poly (N-Vinyl pyrrolidone)
- 12) Poly (ethylene glycol)
- 13) Poly (methyl methacrylate)
- 14) Poly acrylamide
- 15) Poly (vinyl alcohol). [11]

METHOD OF PREPARATION OF NANOCAPSULES:

Nano capsules are prepared by the following methods:

1. polymer absorption/polymerisation method
2. Nano precipitation/solvent displacement method

3. Emulsion-diffusion /evaporation method
4. Solvent evaporation method
5. phase inversion method
6. Double emulsification
7. Emulsion coacervation
8. Polymer coating
9. Layer –by-layer
10. Solvent displacement method or interfacial deposition method

1. polymer absorption/Polymerisation method:

Nanoparticles are formed by polymerising monomers in an aqueous solution followed by placing the drug either by the adsorption of nanoparticles or by dissolving in the medium of polymerization. Ultracentrifugation method, which is utilized for purifying the nano particle suspension, removes various stabilizers and surfactants employed for polymerization. The nanoparticles are then re-suspended in an isotonic surfactant free medium. It has been suggested for making poly butyl cyanoacrylate or poly alkyl cyanoacrylate nanoparticles. It is a actual common method for preparation of nanomaterials. During polymerization, usually, the formation of microemulsion is a very important factor which has been the focus of extensive research worldwide due to its importance in a variety of technological applications. These applications include improved oil recovery, combustion, cosmetics, pharmaceuticals, agriculture, metal cutting, lubrication, food, enzymatic catalysis, organic and bio-organic reactions, chemical synthesis of nanoparticles and nano capsules, etc. [2]

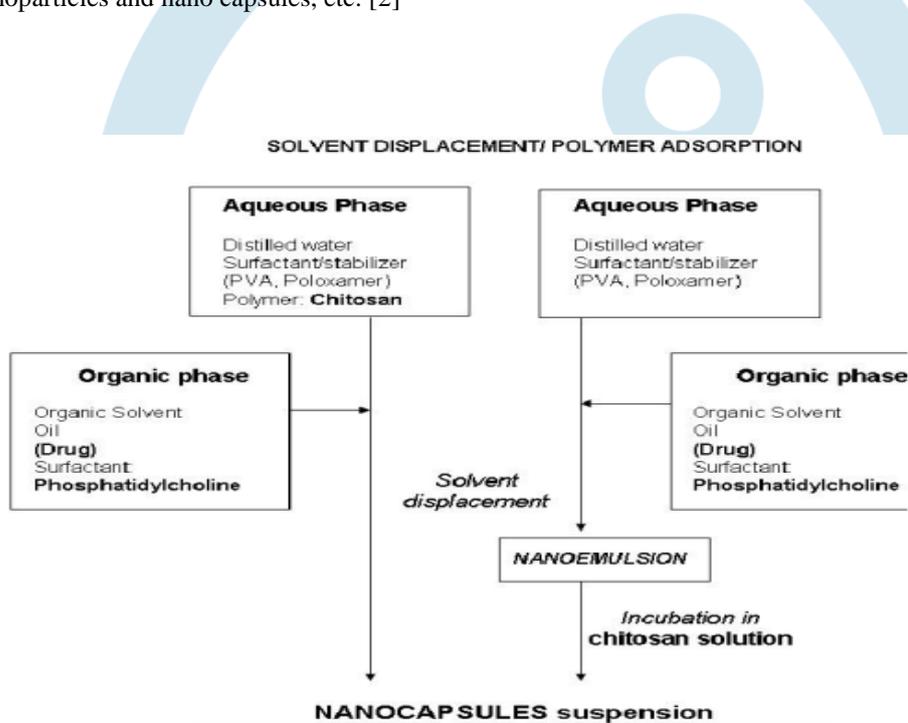


Fig 3: Polymer Absorption/Polymerisation Method

2. Nano precipitation/solvent displacement method:

Nano precipitation is also called solvent displacement method. It includes the precipitation of a preformed polymer from an organic solution and the diffusion of the organic solvent in the aqueous medium in the presence or absence of a wetting agent. The solvent displacement technique allows the preparation of nano capsules when a small volume of nontoxic oil is joint in the organic phase. since the oil-based central cavities of the nano capsules, high loading effectiveness are generally reported for lipophilic drugs when nano capsules are prepared. This method is mostly applicable to lipophilic drugs because of the miscibility of the solvent with the aqueous phase, and it is not an effective means to encapsulate water-soluble drugs. This method has been applied to various polymeric materials such as PLGA PLA PCL and poly (methyl vinyl ether-maleic anhydride) (PVM/MA), This technique was well adapted for the incorporation of cyclosporin A, because entrapment efficiency is high as 98% were obtained. [2] Highly loaded nanoparticulate systems based on amphiphilic h-cyclodextrins to help the parenteral administration of the poorly soluble antifungal drugs Bifonazole and Clotrimazole were prepared according to the solvent displacement method.[7] Highly loaded nanoparticulate systems based on amphiphilic h-cyclodextrins to help the

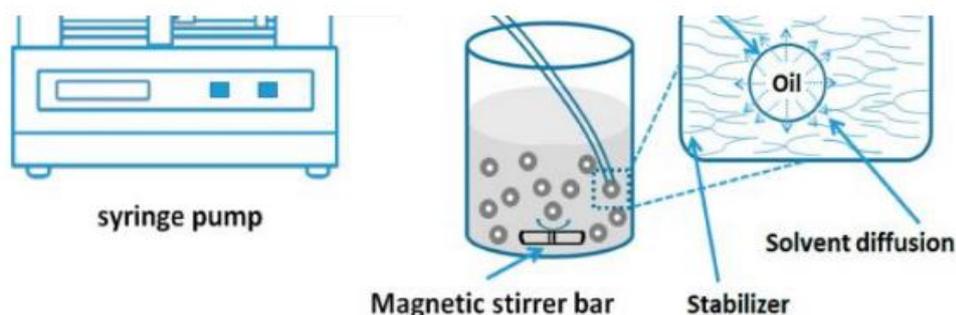


Fig 4: Nanoprecipitation Method

Recommended Composition for preparation of nanocapsules by the nanoprecipitation method.

Material	Suggested composition
Active substance	10-25 mg
Polymer	0.2-0.5% of solvent
Oil	1.0-5.0% of solvent
W/O surfactant	0.2-0.5% of solvent
Stabilizer agent	25 ml
Non-solvent	0.2-0.5% of non-solvent 50 ml

Table1

3. Emulsion-diffusion /evaporation method:

One of the common methods for expressing polymeric nano capsules via nano emulsion is the emulsion– diffusion/evaporation method. It is found on emulsification of the organic phase into an inorganic phase and subsequent elimination of the organic solvent by diffusion into the external phase or evaporation. Nano capsules are formed by a combination of polymer precipitation and interfacial phenomena during the diffusion or an evaporation process.

The polymers that can be used to formulate polymeric nano capsules by emulsion–diffusion method must possess good solubility in an organic solvent, well miscible with water, such acetone, ethanol or ethyl acetate, thereby, removing the organic solvent by diffusion into water. The nano capsules were formed by using acetone and methanol in organic phase, and then purifying by diffusion into the water phase; the hydrophobic amphotericin B was successfully encapsulated with an excellent encapsulation efficiency of $99.2 \pm 1.3\%$. Also, nonpolar solvents such as chloroform or dichloromethane which are immiscible with water may be used in the organic phase in the emulsion-evaporation method. [3]

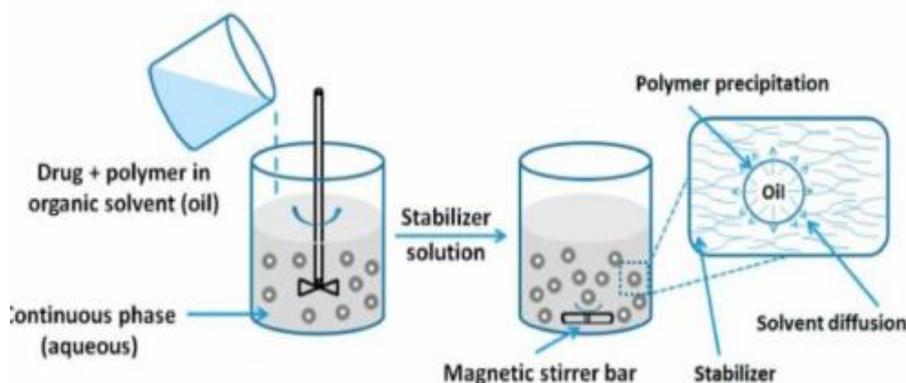


Fig 5: Emulsification Method [21]

Recommended composition for preparation of nanocapsules by emulsion -diffusion method.

Material	Suggested composition
Active substance	10-50 mg
Polymer	1.0-2.0% of inner phase solvent
Oil	2.5-5.0% of inner phase solvent
Inner phase solvent	10 ml
Stabilizer agent	2.0-5.0% of external phase solvent
External phase solvent	40 ml
Dilution phase	200 ml

Table 2

4. Solvent evaporation method:

Solvent evaporation was the first method developed to prepare PNPs from a, In this method polymer solutions are prepared in volatile solvents and emulsions are formulated. In the past, dichloromethane and chloroform preformed polymer [8] were widely used, but are now replaced with ethyl acetate which has a better toxicological profile. The emulsion is changed into a nanoparticle suspension on evaporation of the solvent for the polymer, which is allowed to diffuse complete the continuous phase of the emulsion. In the conventional methods, two main plans are being used for the formation of emulsions, the preparation of single emulsions, e.g., oil-in water (o/w) or double-emulsions, e.g. (water-in-oil)-in-water (w/o)/w. These methods use high-speed homogenization or ultrasonication, followed by evaporation of the solvent, also by continuous magnetic stirring at room temperature or under reduced pressure. At that point, the solidified nanoparticles can be collected by ultracentrifugation and washed with distilled water to remove additives such as surfactants. To end, the product is lyophilized.[2]

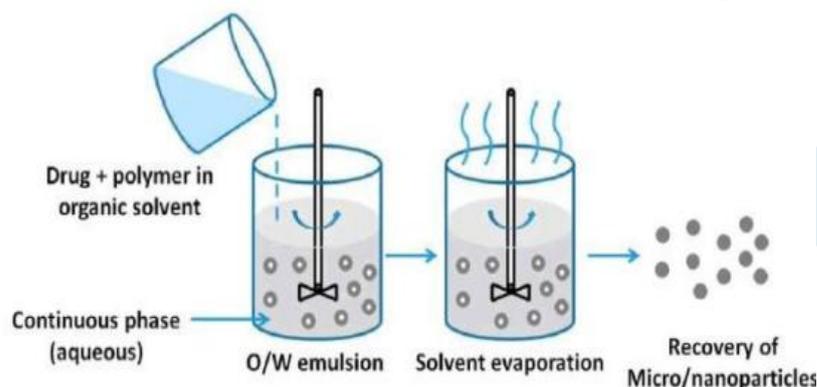


fig 6: Solvent evaporation method

5. Phase Inversion Method:

This method for preparation of silica nano capsules is by inter facial polymerization of nano emulsions which are prepared by the phase inversion temperature (PIT) method. This is a low-pressure homogeniser. The nano emulsions were prepared with decant as the oil phase, in which tetra ethoxylate (TESO) was dissolved with an ethoxylated alcohol as the surfactant. The hydrolysis and polymerization of the TESO was performed under basic and acidic conditions using HCl and ammonia, respectively. The obtained nano capsules have an average size between 100 and 300 nm, which consists of an oil core(decant) and silica shell, which were characterized using dynamic light scattering, Fourier transform infrared spectroscopy (FTIR), highresolution scanning electron microscopy (HR-SEM) and by fluorescence of an encapsulated aloe ant chromic dye. The capsules could be positively or negatively charged by adsorption of ionic surfactants after they were formed [2]

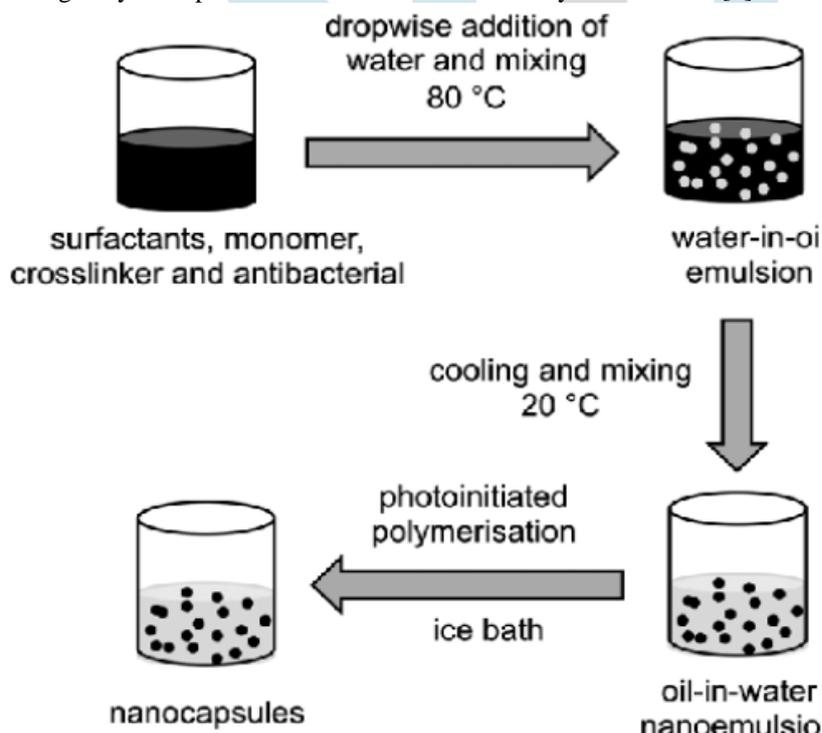


Fig 7: Phase Inversion Method

6. Double Emulsification:

Double emulsions are complex hyperdispersed systems called “emulsions of emulsions”, they are classified into two major types: water-oil-water emulsion (w/o/w) and oil-water-oil emulsion (o/w/o). Therefore, the dispersed phase is itself an emulsion and the inner dispersed globule/droplet is separated from the outer liquid phase by a layer of another phase. Double emulsions are usually prepared in a two-step emulsification process using two surfactants a hydrophobic one considered to stabilize the interface of the w/o internal emulsion then a hydrophilic unity to steady the external interface of the oil globules for w/o/w emulsions. for preparation of nano capsules, the principle of double emulsion formation, specifically of the w/o/w type, is related with the principles of together nanoprecipitation and emulsion diffusion methods. In this case, in the prime w/o emulsion the oil is changed by an organic phase containing a solvent that is completely or partially miscible in water, the film-formed polymer and a w/o surfactant. Then the water holding a stabilizing agent is additional to the system to obtain the water in organic in water emulsion. Though, in this step, particle toughening is found through solvent diffusion and polymer precipitation. Water is commonly added to the double emulsion in order to achieved full solvent diffusion. According to Khoi and Yaghoobi, surfactants play a dual role in emulsions: as a film former and a barrier to drug release at the internal interface, and as a steric stabilizer on the external interface.

Suggested composition for preparation of nanocapsules by the double emulsification method.

Material	Suggested composition
Inner aqueous phase Active substance Water	Variable (0.5-25mg) 0.15-0.5ml
Organic phase polymer W/O surfactant solvent	5-10% of organic phase solvent 5-7% of organic solvent 1.5-5 ml
External aqueous phase Stabilizer agent Water	1-5% of external aqueous phase solvent 2-5 ml
Dilution phase (optional) Stabilizer agent Water	1.5% of dilution phase solvent 50-100 ml

Table 3

It was found that drug encapsulation efficiency and average particle size are affected by altering the type and concentration of together the w/o emulsion and the stabilizing agent. A composition base for preparation of nano capsules at laboratory-scale by the double emulsification method (size about 150–200 nm) is provided in Table 3. In the organic phase, ethyl acetate, methylene chloride and dichloromethane have remained used as solvents besides biodegradable polyesters, like PCL, PLA and PLGA have been frequently used. About o/w surfactants, sorbitol esters are chosen. Regarding the external aqueous phase, the stabilizing agents greatest frequently used are PVA and polysorbates. [6]

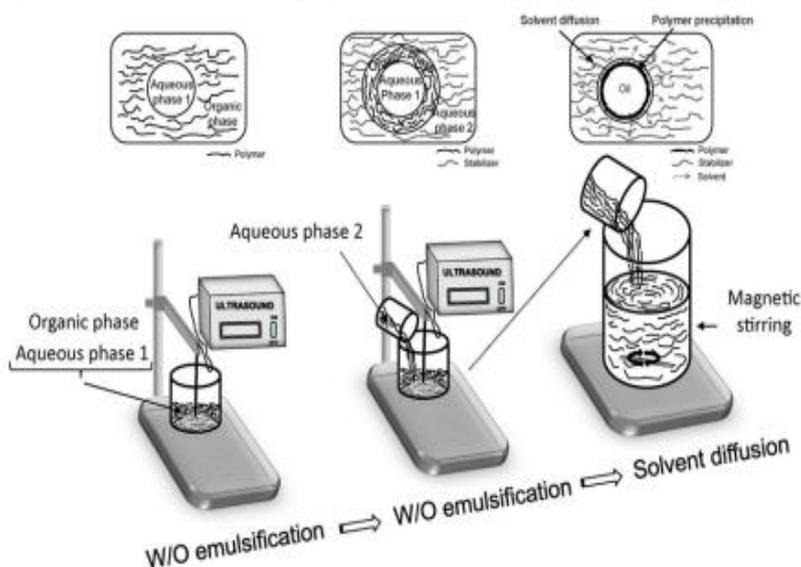


Fig 8: Set-up used for preparation of nano capsules by the double emulsification method.

7. Emulsion coacervation: The emulsion-coacervation process is mainly presented as a strategy for nano capsules preparation from naturally occurring polymeric materials. Up to now, sodium alginate and gelatine have been used though synthetic polymeric materials could be used for this purpose. The procedure involves the o/w emulsification of an organic phase (oil, active substance and active substance solvent if necessary) with an aqueous phase (water, polymer, stabilizing agent) by mechanical stirring or ultrasound. Then, a simple coacervation process is completed by using either electrolytes. In the addition of a water miscible non-solvent or a dehydration agent as done by Krause and Rohde Wald (1985) with a gelatine–isopropanol–sodium

sulphate system or by temperature modification as done by Latter et al. (2008) with the application of triblock terpolymer in gold nano capsule synthesis.

Finally, the coacervation process is complemented with additional crosslinked steps that make it possible to obtain a rigid nano capsule shell structure (fig 9) Nano capsule formation by the emulsion-coacervation method uses the emulsion as a template phase and the formation of a coacervate phase that causes polymer precipitation from the continuous emulsion-phase to form a film on the template forming the nano capsule. Additionally, it can be stabilized by physical intermolecular or covalent cross-linking, which naturally can be completed by altering pH or temperature, or by adding a cross-linking agent.

Probably the critical stage in preparation of nano capsules by the emulsion-coacervation method is coacervate phase formation. the polymer dissolved in water is bounded by water molecules that solvate its functional groups, typically through hydrogen-bonding and van der Waals forces that prevent attraction among chain segments in close proximity by interchain H-bonds, or van der Waals or opposing ionic forces. Thus, the coacervating agents lower the solvation of dissolved polymers and make thin solvated shell. [6]

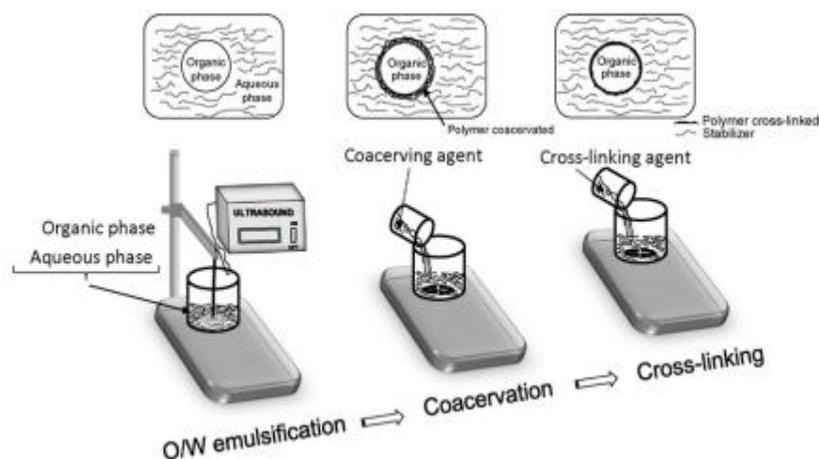


Fig 9: Set-up used for preparation of nano capsules by the emulsion-coacervation method.

8. Polymer coating:

A polymer-coating method in which the first step is to prepare the nano emulsion template and then coat it by polymer deposition on the water/oil nano emulsion surface. The polymers are added in the continuous phase and their precipitation onto the nano emulsion droplets is triggered by solvent evaporation, as opposed to the emulsion coacervation method. In their procedure (Fig. 10), they start from an organic phase composed of the active substance, oil, surfactant (lecithin) and acetone as solvent; an aqueous phase containing the stabilizing agent and an aqueous polymer-coating solution. The organic and aqueous phases are mixed under moderate stirring and the o/w nano emulsion is formed by solvent displacement. The solvents are subsequently evaporated under vacuum until reaching a specific volume and the nano emulsion is finally coated by the polymer by simple incubation in the polymer solution. The nano capsule formation mechanism is mediated by the ionic interaction between the negatively charged phospholipids and the positively charged chitosan molecules. As in the emulsion-coacervation method, taking into account the limited amount of research and their different methodological strategies, it is premature to establish general criteria for the materials and compositions that could be employed.[6]

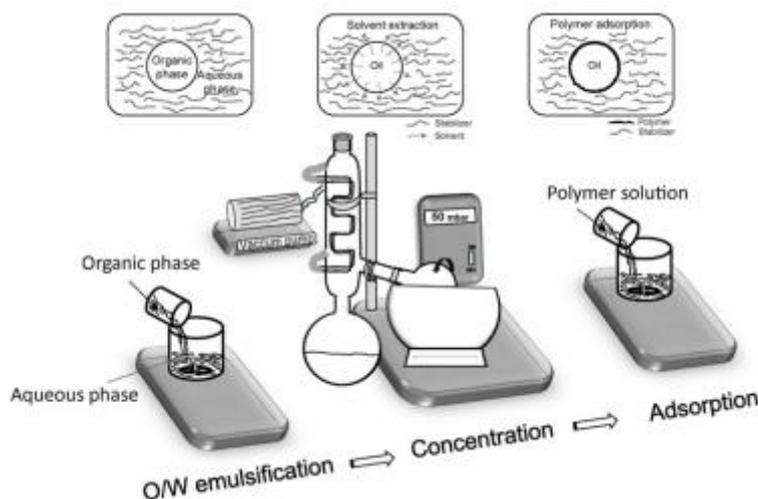


Fig 10: Set-up used for preparation of nano capsules by the polymer-coating method.

9. Layer –by-layer:

The layer-by-layer method is mainly used for the colloidal particle preparation makes it possible to get vesicular particles, called polyelectrolyte capsules.[25] The layer-by-layer get-together process developed by Sukhorukov et al. (1998) for colloidal particle preparation makes it possible to get vesicular particles, called polyelectrolyte capsules, with well-defined chemical and structural properties. To sum up, the mechanism of nano capsule formation is based on irreversible electrostatic attraction that leads to polyelectrolyte adsorption at supersaturating bulk polyelectrolyte concentrations.

This method needs a colloidal template on which is adsorbed a polymer layer either by development in the polymer solution, subsequently washed, or by decreasing polymer solubility by drop-wise addition of a miscible solvent (Radtschenko et al., 2002a). This procedure is then repeated with a second polymer and multiple polymer layers are deposited sequentially, one after another. But, this problem has been overcome by ultra-sonic treatment of aqueous suspensions to decrease the size of individual drug particles to nano-scale (100–200 nm). They are then stabilized in solution by applying layer-by-layer coating by ultra-sonic treatment and thin polyelectrolyte shells are assembled on their surfaces.

Thus, although research using this strategy has greatly improved the technique, it is acknowledged that the high number of assembly steps involved is quite complex and time consuming, particularly for the synthesis of thick-walled polymer nano capsules.[6]

10. Solvent displacement method / interfacial deposition method:

Interfacial polymerization is an alternative to bulk polymerization of condensation polymers, which would require high temperatures. It includes of two immiscible solvents, in which monomer in one solvent instantaneously reacting with monomer of the other solvent or it may depend on the time scale. Higher molecular weights of monomers are obtained then it is more likely to stumble upon a growing chain than the opposing monomer. For example, the nano capsules can be formulated by using the aqueous core containing oligonucleotides of isobutyl cyanoacrylate in a W/O emulsion. The resulting nano capsules are then purified by ultracentrifugation followed by resuspending in water to yield a dispersion of aqueous core nano capsules. Equally solvent (organic phase) and non-solvent phases (aqueous phase) are used in the synthesis of nano capsule. Solvent phase containing solvents (ethanol, propanone and hexane), polymers (natural or synthetic polymer), the drug molecule and oils. On the other pointer, the non-solvent phase containing of a non-solvent or a mixture of nonsolvent for the polymers, supplemented with one or more naturally occurring or synthetic surfactants. The solvent is an organic medium, while the non-solvent is mainly water. In the solvent displacement method, the nano capsules are obtained as a colloidal suspension formed when the organic phase is added slowly with continuous moderate stirring to the aqueous phase. In the Solvent displacement method, commonly used biodegradable polymers are poly-ε-caprolactone (PCL).[4]

APPLICATIONS:

1. Agrochemicals
2. Anti-inflammatory drugs
3. Antiseptics
4. Cosmetics
5. Diabetes
6. Nanocapsules for cancer
7. Nanocapsule for Topical use [1]

ADVANTAGES:

- ✓ Higher dose loading.
- ✓ Decrease irritation of drug at site of administration.
- ✓ More protection from degradation during storage & after administration.
- ✓ Place specific action.
- ✓ Rise bioavailability of drug.
- ✓ Control & sustain release of the drug at the site of localization.
- ✓ The system can be used for many routes of administration including, oral, Nasal, parenteral, intraocular etc. [12]

DISADVANTAGES:

- Very costly formulation with no low yield
- Productivity is more difficult. As an industrial application, technology transfer to commercial production is very difficult
- Reduced ability to adjust the dose
- Highly sophisticated technology
- Requires skills to manufacture
- Stability of dosage form is big issue owing to its nano size
- Recycling is very expensive [14]

BENEFITS OF NANOCAPSULES:

- Receptors can be added without changes to drug structure.
- Minimize drug degradation.
- Increase drug bioavailability

- Dosage for drugs can be decreased by 10,00.[13]

IMPORTANT CAPSULES PROPERTIES:

Naturally, with the application as a drug delivery system in mind, the physical and chemical properties of the individual capsules become crucial characteristics. Fortunately, all preparation procedures offer means to vary the key parameters which mainly consist in the capsule radius distribution, the capsule surface, the thickness and the permeability of the capsule membrane and its thermal or chemical decomposition. In the next, the determination of these capsule parameters is described [15]

Capsule Radius:

Generally, the radius of nanocapsules is also small to be directly accessible by a light microscopic measurement. But light microscopy may be used for an indirect determination of the size of nanoparticles in dispersion. A dark-field light microscope, prepared with a video camera and an automatic image analysis system allows for efficient particle tracking of capsules with radii between 50 and 500 nm. Simultaneous observation of up to 50 particles is repeated several times, resulting in a particle size histogram.[16]

The Capsules Surface:

The outer capsule surface represents a very important feature of a capsule system as it is directly linked to the immunological response in a living organism. Now, the most promising way to minimize the immunological reaction is to use block copolymer surfactants (e.g. ABA- block copolymers after ethylenoxide and propyleneoxide units) which adsorb to the capsule surface but undergo a rapid exchange with the surrounding liquid medium. The rapid exchange process professionally covers the solid particle from most mechanisms of recognition and simultaneously stabilizes the aqueous dispersion. As these surfactants work as nonionic stabilizers, they are not unfair by the interaction with ionic solutions. The method of rapid exchange on the particle surface can be observed with methods of nuclear magnetic resonance (NMR).[17]

Thermal Or Chemical Decomposition:

The processes leading to capsule decomposition may be manifold. They consist of chemical decomposition by the hydrolytic degradation of the polymer, by oxidation or by enzymatic action in a living organism as well as physical decomposition caused by shear forces, heat or sonic disruption. In all cases, the capsule decomposition finally leads to the release of the capsule contents. The corresponding loss of the solid capsule constituents can be followed by solid state NMR.[18]

The results clearly show that the contribution of the solid material continuously decreases, while the overall shape and the size of the solid body are conserved. At the same time, traces of molecular fragments of the polymer appear in the solution. This is in accordance with the model of a disintegrating solid sphere which basically remains intact in its outlines, while at the same time suffering increasing erosion, leading to rapid molecular exchange through the remaining capsule wall.

CHARACTERIZATION OF NANOCAPSULES:

a) Morphology Of Nanocapsules:

The morphology of the nanocapsule can provide the information about the functional and physicochemical properties.

1) Electron Microscopy:

Electron microscopy is common method to study the structure of nanocapsule (<1000nm). There are two basic microscopy techniques transmission electron and scanning electron microscopy. The transmission electron microscopy gives preferred determination over scanning electron microscopy in light of the fact that the vitality of the electron beam in transmission electron microscopy is higher; it is capable of creating images with a magnification of 10³ to 10⁶ and a resolution smaller than 1nm. The scanning electron microscopy is able to provide images from the surface of the materials with a magnification of 10 to 500000 at a resolution of less than 1-20nm.

2) Electric charge of nanocapsule:

Measuring the surface charge of nanocapsule is necessary to determine their stability, physicochemical and functional properties, encapsulation efficiency. Zeta-potential is the common technique for describing the surface charge of nanocapsule due to better representation and simple measurement of the electrical characteristics Zetapotential measurement reveals information about the dispersion, aggregation or flocculation needed for improving the dispersions emulsions and suspensions.

b) Physicochemical properties of nanocapsule:

The physicochemical state of nanocapsule can provide fundamental information about their application, stability, functional properties, and resistance.

1) X-ray diffraction:

Provides information about the physical state of the atomic and molecular structure of crystal.[19]

2) Differential Scanning Calorimetry:

This technique is use for the measuring changes in enthalpy of samples that are expose to temperature variation like the heating or cooling process. This method can also provide the information about the glass transition temperature, heat capacity and melting point.

3) Fourier transform infrared spectroscopy:

Fourier Transform Infrared spectroscopy provides an infrared spectrum of absorption or emission of a solid, liquid or gas. It is used for determination of interactions bonding and complex formation in colloid delivery system.[20]

c) Stability of Nanocapsule:

Stability of nanocapsule is necessary to evaluate the storage condition of the nanocapsule and applying them in targeted formulation.

1) Storage stability testing:

Storage stability is the most common technique for determining stability of nanocapsule in many formulation. In the storage stability testing it is possible to investigate the influence of ambient conditions on the stability of Nano system by changing the factors like temperature and air condition during storage. The stability indices including creaming index, Zetapotential, encapsulation efficiency, turbidity and viscosity are measured during prespecified storage time. [20]

3) Accelerated stability testing:

The accelerated technique is a method of measuring the stability of the colloidal delivery system in short time as well as prediction of their long-term stability. [19]

CONCLUSION:

The main goal of this review was to describe the different preparation techniques available for production of polymeric nanocapsules. It was observed that preparing PNCs is a state-of-art technology that requires a suitable technique among the various possible methods. Nanocapsules preparation methods have been marked by three aspects: 1) need for less toxic reagents 2) simplification of the procedure to allow economic scale up 3) optimization to improve yield and entrapment efficiency. Limitations like one particular process or technique is not suitable to all drugs, post preparative steps, such as purification and preservation, incomplete or discontinuous film, inadequate stability of certain active components are remained to solve. Despite these technological challenges, nanocapsules have been showed great promise for the development of drug delivery system. They also have the efficient applications in various fields of the agrochemical, waste water treatments, genetic engineering, cosmetics, cleaning products, as well as in adhesive component. In upcoming future, they provide the novel effective drug delivery system.

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